Bronchioloalveolar Carcinoma of Lung In A Married Couple

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A married white couple had developed an identical solitary bronchioloalveolar carcinoma of the posterior segment of the right upper lobe of the lung. Attention was focused on a previous viral lung infection and other environmental factors which are etiologically related to cancer of the human lung. Several favorable and unfavorable factors in the prognosis of the spouses are discussed.

Evidence for the role of a previous viral lung infection and other environmental factors in cancer of the human lung is limited. This case report describes white spouses who developed histologically identical bronchioloalveolar carcinoma in the same bronchopulmonary segment. The couple shared some common features that they had previous viral pulmonary infections off and on for more than one year's duration. They developed carcinoma of the lung in their seventh decade. A solitary coin lesion of identical shape, cell type and anatomical location was simultaneously found in both of them. They were admitted for identical examinations and received similar operations on the same day. They had some important differences, however. The husband smoked one pack of cigarettes daily, while the wife was a non-smoker. The husband's blood type is group B, the wife's was group A.

Review of the literature has not shown any previous report concerning identical bronchioloalveolar carcinoma in spouses, although hundreds of cases have been reported by Mortiz (1950)[23], Storey (1953)[37], Waston (1966)[49] and Marcq (1973)[27] since Malasez in 1876 first described the bronchioloalveolar carcinoma.

Bronchioloalveolar carcinoma constitutes about 5% of all primary lung cancer. It would be of interest to establish the exact occurrence of this rare type of primary lung carcinoma in married couples.

Case Report

Mr. P.C. (husband)-A 76 year old white male was admitted on March, 15, 1975. He had smoked one pack of cigarettes a day since the age of 16. He had worked in a chemical plant which was dealing

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with chromium for 22 years. He had been a shepherd for about 10 years in Italy before he immigrated to U.S. in 1921. He was in good health before 1965, but underwent a transurethral resection for benign prostate hypertrophy in December, 1965. He was admitted with high fever and multiple fine moist rales in both lungs in January, 1966. However, there was no infiltration or pleural effusion shown on his chest x-ray film. He had another transurethral resection for papillary carcinoma of the urinary Bladder in June, 1971. A chest x-ray at that time revealed pulmonary fibrosis. Since then he continued to cough up about 90 ml of yellowish sputum early each morning. In January 1975, his cough became more productive and two months later he was admitted because of chest pain, dyspnea and weakness. A chest roentgenogram in posteroanterior projection (Fig IA) demonstrated a well circumscribed, roud area of increased density approximately 3 cm in diameter localized in the posterior segment of the right upper lobe of the lung. Spiculations were noted at the margin of the mass as seen in the tomogram both in anteroposterior projection and lateral projection. Sputum cytology showed a group of dysplastic cells. Bronchoscopy and biopsy were essentially negative. Mediastinoscopic biopsy and scalene node biopsy were also negative.

On March 31, 1975, the patient underwent forzen section following a right upper and middle lobes lobectomy. The operative specimen consisted of a tumor 3 cm in diameter which arose from the posterior segment of the right upper lobe. There was no chest wall attachment but the tumor had extended to the visceral pleura. (Fig. IIA). Histological exaimination showed a bronchioloalveolar carcinoma with an alveolar-papillary and alveolar-solid pattern interstitial fibrosis. The margins of section were free of tumor. Unfortunately, the patient expired due to combined respiratory and renal failure six weeks postoperatively and autopsy at that time showed no evidence of recurrent tumor.

Mr. T.C. (wife)-A 73 year old white female was admitted on March 15, 1975 with the chief complaints of intermittent chest and low back pain with occasional cough of about 12 months duration. There was no history of blood in the sputum. She had immigrated to the U.S. with her husband, but was a non-smoker, and neither worked as a shepherdess nor had known exposure to the chromium products at her husband's chemical plant. She received a hystero-oophorectomy in 1934 for a uterine myoma, a cholecystectomy in 1970 and a hemorrhoidectomy in 1873. A chest roentgenogram in the posteroanterior density approximately 3 cm in diameter localized in the posterior segment of the right upper lobe of the lung. This solitary lesion showed a circumscribed margin in the tomograms. Sputum cytology showed a group of mildly dysplastic cells. Bronchoscopy and biopsy, mediastinoscopic biopsy and scalene node biopsy was all essentially negative.

On March 31, 1975, she underwent exploratory thoracotomy with

forzen section followed by a right upper and middle lobes lobectomy. The operative specimen consisted of a tumor 3 cm in diameter arising from the posterior segment of right upper lobe of the lung, the tumor extended to the visceral pleura but there was no chest wall attachment (Fig.IIB). Histological examination showed a bronchioloalveolar carcinoma with alveolar-papillary and alveolar-solid pattern intermingled with interstitial fibrosis. There were no lymph node metastasis and no blood vessel invasion. Again, the margins of resection were free of tumor. The patient is now 26 months postoperatively without evidence of recurrence.

Discussion

The above mentioned man had been subjected to various environmental pollutants including chromate. These, together with viral carcinogen, smoking and "jaagsiekte"-sheep viral infectious disease, probably increased the risk of occurrence of pulmonary neoplasms in this patient. However, the spouses had in common only the factors of repeated viral lung infection, pulmonary fibrosis and senile changes. It is reasonable that those three factors be considered to be implicated in the pulmonary carcinogenesis of the spouses.

The gross and microscopic characteristics of the bronchioloalveolar carcinomas were similar in the couple. The tumors arose from the peripheral bronchiole of posterior segment of the right upper lobe (Fig. IIA, Fib. IIB) with alveolar-papillary and alveolar-solid pattern bronchioloalveolar carcinoma intermingled with interstitial fibrosis. The alveolar structures were well preserved as showed in Fig. IIIA and Fig. IIIB. No invasion of lymph nodes or blood vessels was observed through examinations by Hematoxylin and Eosin tissue staining.

Doll (1955)[13] reported that chromium workers have an increased risk of lung cancer between 14 to 80 times that of the general population. Mr. P.C. had urinary bladder and lung cancinomas, while Mrs. T.C. only had lung carcinoma. Since the wife did not work at her husband's chemical plant, it seemed that chemical carcinogens were not responsible for the identical lung carcinogenesis for the couple.

Cunningham (1958)[10] described a lesion similar to adenomatosis in sheep (jaagsiekte) which is found in man as bronchioloalveolar carcinoma of the lung. It is highly suspected to be of viral etiology. Although, there is no strong evidence to indicate that bronchioloalveolar carcinoma in man is an infectious disease, a few reported cases of human bronchioloalveolar carcinoma had been exposed to jaagsiekte. Again, the husband had been a shepherd before 1921, and the wife had never been a shepherdess.

Weiss (1972)[50] stated that bronchioloalveolar carcinoma showed a dose response relationship to cigarette smoking. Watson (1973)[51] remarked that a viral infection may be a more important factor than

cigarettes in patients developing bronchioloalveolar carcinoma. The husband smoked a pack of cigarettes daily, while the wife did not smoke at all.

Burch (1963)[7], Tokuhata (1964)[47], Brisman (1967)[9] had drawn the conclusion that a familial aggregation of malignant disease in man can generally be attributed to the genetic factor with Mendelian dominance of incomplete penetrance. The pedigrees of the families of both spouses showed neither evidence of consanginous marriage nor inherited susceptibility to carcinoma.

It appears to be unlikely that those factors (Chromate Exposure, genetic carcinogenesis, cigarettes smoking and shepherding) play an important role in the carcinogenesis of these spouses.

Rabotti (1965)[33] in an animal experiment study showed that virus might be regarded as a possible environmental extragenetic factor in the development of lung tumors in mice. Smith (1949)[35] carried out tests to show a virus in a transplantable tumor of mouse lung origin. Leuchtenberger (1963)[22] concluded that influenza virus would appear to be an "infectious" RNA virus which under certain conditions might be implicated in the malignant transformation of cells. Rosenblatt (1963)[31] reported that specific epithelial degeneration (ciliocytophoria) and malignant changes of viral respiratory infection, especially that of bronchitis, is of the greatest importance in the etiology of lung carcinoma. Furthermore, Watson (1966)[49] examined a series of terminal bronchioloalveolar carcinoma of lung and found that a high percentage (17%) of the patients with this morphological type of disease gave a past history of one or more attacks of viral pneumonia, atypical penumonia, or influenza. Although, Brisman(1967)[9] proposed chromosomal evaluation to verify a possible viral carcinogenesis, we did not have chromosomal evaluation to indicate whether these two individuals had normal white blood cell karyotypes or not.

Haddad (1968)[19] reported that cases of diffuse interstitial pulmonary fibrosis are prone to the development of lung carcinoma. Spain (1957) postulated terminal bronchioloalveolar carcinoma may develop in an environment of chronic inflammation or interstitial pulmonary fibrosis in which alveolar epithelial hyperplasia has occurred. Meyer (1965) pointed out that most of the lung carcinoma associated with honeycombing (atypical epithelial proliferation) were in the upper lobe of lung and 31% were adenocarcinoma in type and 83% arose in the periphery of lung.

On the other hand, Sirtori (1964)[40] carried out mice experiment studies concluding that the senile lung's decreased elasticity could favor the stagnation of inhaled carcinogens, he also felt that inhaled carcinogens or cigarette smoke provoke lung cancer only in association with the influenza virus, and therefore the greater susceptibility of senile lung to the influenza virus can contribute to its greater susceptibility to lung cancer. He further indicated that senility in itself is a precancerous condition because there are certain morphological similarities between senile cells and tumor cells.

In view of the above evidence relating to common carcinogenic factors for the identical lung carcinomas in the two spouses, one can easily concluded that carcinogenesis generally can be attributed to the repeated repiratory tract viral infection associated with homogeneous environmental conditions in the lung such as pulmonary fibrosis and senility.

The spouses are remarkable not only for the presence of identical lung lesions and identical cell types and location, but also for several factors which make their prognosis both favorable and unfavorable:

(1) Both had resectable solitary lesions with no involvement of scalene lymph node, cervicomediastinum lymph node or central bronchus.

(2) These bronchioloalveolar carcinomas were localized at the posterior segment of right upper lobe of the lungs.

(3) Both were free of tumor involvement at the postresection bronchus and lung parenchyma.

(4) Each patient had an identical bronchioloalveolar carcinoma.

(5) There was no evidence of lymph node and blood vessel invasion.

(6) Preoperatively, each had mild or severe chronic pulmonary obstructive disease.

Munnel (1966)[25] reviewed the literature and together with his own series concluded that in solitary lesions of bronchioloalveolar carcinoma, the 5 year postoperative survival rate of lobectomy is usually greater than 60% while that of diffuse lesions in almost 0%. Belgrad (1962)[6] reported that a single foçus of bronchioloalveolar carcinoma usually can remain localized at least a year during which surgical excision of the tumor may eradicate the disease. The solitary lesion is another favorable factor for the couple in terms of its unicentric origin as described by Storey (1953)[37].

In regard to the favorable prognosis due to the lack of lymph node and blood vessel invasion in the spouses, Reinhoff (1965)[32] remarked that the long term survival rate of lung carcinoma patients with the bronchioloalveolar type of carcinoma was significantly favorable (87%); and that with the absence of lymph node and blood vessel involvement, the 5 year survival rate was 5 times better than those with lymph node and blood vessel involvement.

Fadhi (1963)[16] stated that there is a correlation between blood group A and the patient with more than one primary neoplasm. Of the spouses, Mrs. T.C. with group A blood type had only one primary bronchioloalveolar carcinoma of the lung. Mr. P.C. with group B had one primary bronchioloalveolar carcinoma of the lung and one papillary adenocarcinoma of the urinary bladder. There was no such correlation demonstrated in this case.

Mrs. T.C., now 26 months postoperative, is alive and well, but Mr. P.C. expired 6 weeks postoperatively because of combined respiratory and renal failure. So far there has been no evidence of

recurrence or metastasis noted. Preoperatively, the wife had mild chronic obstructive pulmonary disease, while the husband had severe chronic obstructive pulmonary disease which did not show any evidence of pulmonary function improvement following administration of a bronchodilator.

Right upper and middle lobe lobectomy for lung cancer patients like Mr. P.C. who are afflicted with severe chronic obstructive pulmonary disease is just not feasible at this time, because in such patients, the remaining lung will be unable to support life. If we extrapolate one step further, only lung transplantation could save the life of a patient such as Mr. P.C.

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Legends

Fig.IA. A chest roentgenogram of Mr. P.C.'s in posteroanterior projection demonstrated a well circumscribed, round area of increased density approximately 3 cm in diameter localized in the posterior segment of the right upper lobe of the lung.

Fig.IB. A chest roentgenogram of Mrs. T.C.'s in posteroanterior projection demonstrated a relatively faintly increased density approximately 3 cm in diameter localized in the posterior segment of the right upper lobe of the lung.

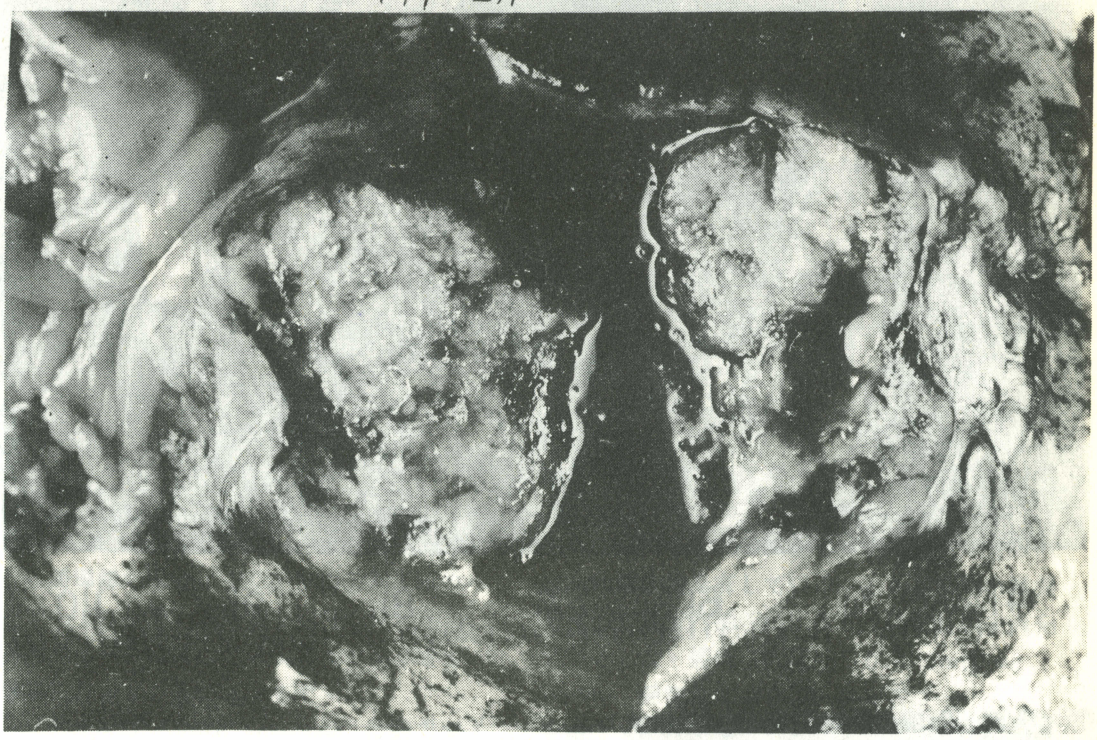
Fig.IIA. Gross section of the lung lesion of Mr. P.C.'s which showed no chest wall attachment but the tumor had extended to the viceral pleura.

Fig.IIB. Gross section of the lung lesion of Mr. T.C.'s which showed no chest wall attachment but the tumor had extended to the viceral pleura.

Fig.IIIA. Microscopic findings of lung lesion of Mr. P.C.'s which showed an alveolar-papillary and alveolar-solid pattern bronchioloalveolar carcinoma intermingled with interstitial fibrosis. (Hematoxylin and Eosin stain 100 x).

Fig.IIIB. Microscopic findings of lung lesion of Mrs. T.C.'c which showed an alveolar-papillary and alveolar-solid pattern bronchioloalveolar carcinoma intermingled with interstitial fibrosis. (Hematoxylin and Eosin stain 50 x).

FIG IIA



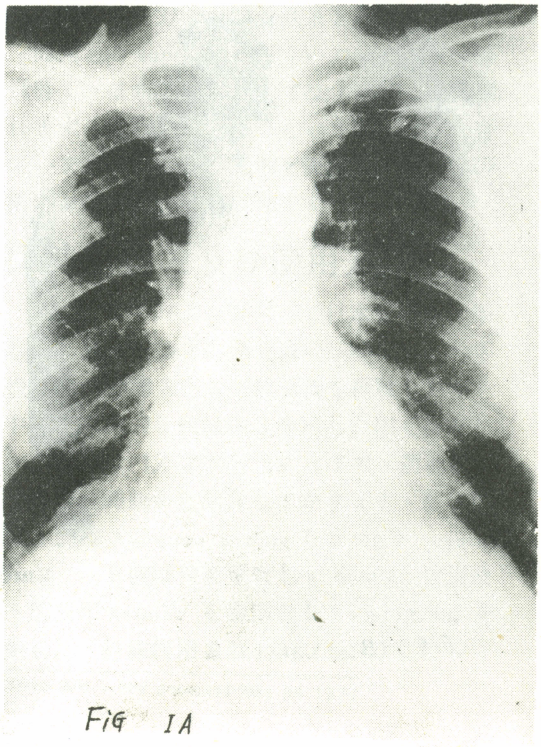


FIG IA

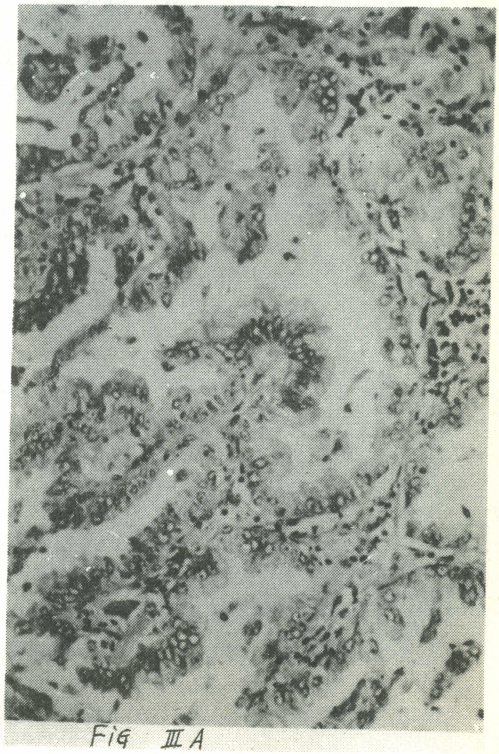
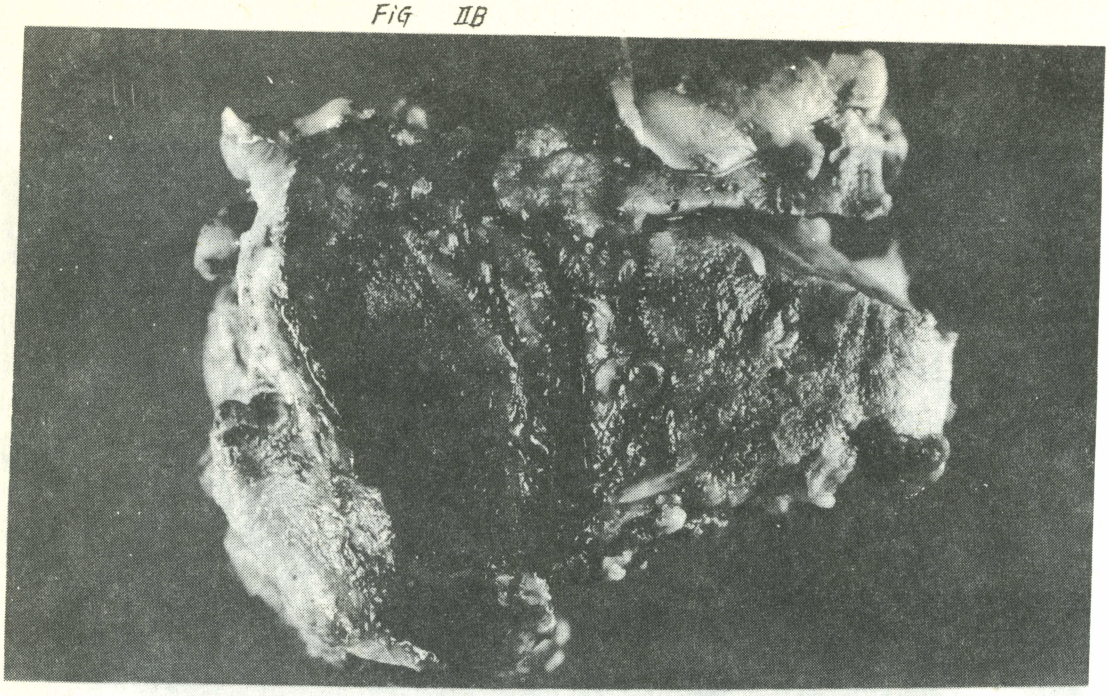
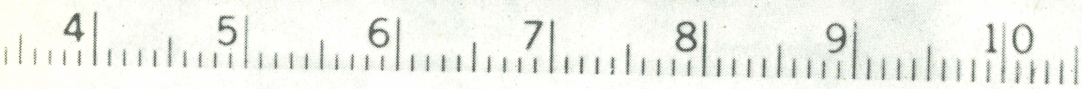


FIG IIIA

Fig IIB





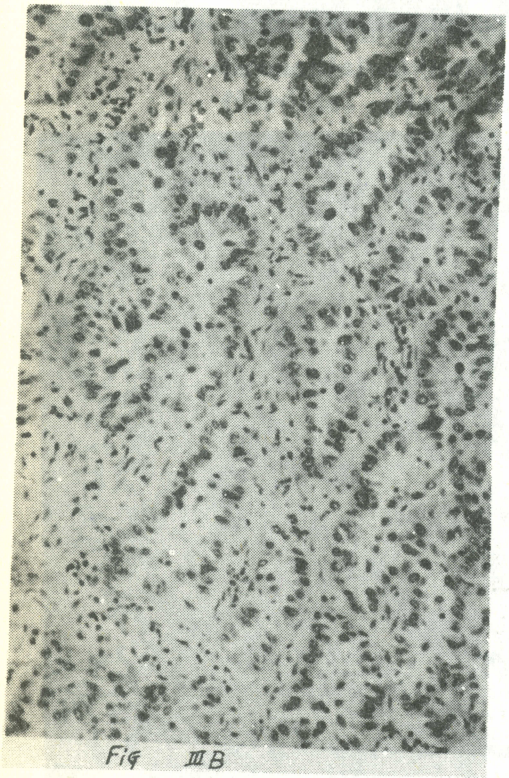


Fig IIIB

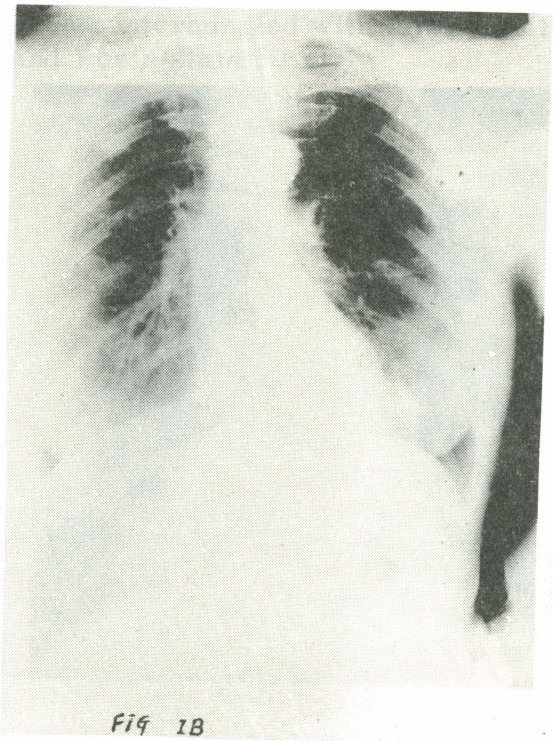


Fig IB